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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,591	10/31/2003	David E. Wolf	205-009US1	1643

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EXAMINER	
RAMILLANO, LORE JANET	
ART UNIT	**PAPER NUMBER**
1797	

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12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,591	WOLF, DAVID E.	
	Examiner	Art Unit	
	Lore Ramillano	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *25-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/31/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. In applicant's reply filed on 9/20/07, applicant amended claims 12 and 23. Claims 25-46 are withdrawn. Claims 1-24 and 47-48 are under examination.

Response to Amendment

Declaration

2. The declaration under 37 CFR 1.132 filed on 9/20/07 is sufficient to overcome the rejection of claims 1-19, 24, 48 and 49 under 35 U.S.C. 102(e) as being anticipated by Wolf '503 in light of Chen; and under 35 U.S.C. 103(a) as being unpatentable over Wolf '503, in light of Chen, and in view of Chick.

Claim Objections

3. The objection to claims 25-45, and 47 is withdrawn.

Claim Rejections - 35 USC § 112

4. The rejection of claims 12, 48, and 49 under 35 U.S.C. 112, second paragraph, is withdrawn.

Prior art rejections

5. In light of applicant's amendment and arguments, the rejection over the prior art is withdrawn. New rejections follow.

Claim Rejections - 35 USC § 103

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. **Claims 1-6, 10-15, and 47** are rejected under 35 U.S.C. 103(a) as being unpatentable over Skjak-Braek et al. ("Skjak-Braek," WO 91/07951) in view of Morrison et al. ("Morrison," US 6099864) and Thatcher et al. ("Thatcher," US 6218112).

Skjak-Braek discloses a core comprising hydrogel (i.e. p. 9, line 13 to p. 10, line 3); a semipermeable coating (i.e. PLL) surrounding the core, which has a molecular weight of less than 20,000 (another way of describing, "weight average molecular weight," p. 10, lines 4-15); a biocompatible coating surrounding the semipermeable coating (i.e. p. 10, lines 16-24); a diameter no greater than 3 mm (i.e. p. 18, lines 27-34); and the sensor exhibiting less than 1 mole % leakage when stored for two weeks at 37 degrees Celcius in pH 7.4 10 mM HEPES/0.15 M saline solution.

Skjak-Braek does not specifically disclose having a fluorescence reagent disposed in the core. Morrison discloses a microcapsule comprising an outer polymer membrane (122, fig. 1) that encloses at least two immiscible liquid phases. Morrison further discloses that one or more phases of his microcapsule comprises fluorescent molecules consisting of fluoresceins, cyanins, naturally fluorescent molecules, rhodamines, and others excited between 260 and 700 nanometers. (i.e. column 34, lines 28-41; column 23, lines 3-17). It would have been obvious to a person of ordinary skill in the art to modify Skjak-Braek's microcapsule by incorporating fluorescent molecules in the microcapsule because such molecules would provide a useful means for allowing radiological monitoring during intravascular delivery, and for enabling accurate measurements of the drug compartment volumes (i.e. Morrison, column 29, lines 31-59).

Furthermore, Skjak-Braek does not specifically disclose that the semipermeable coating has a polydispersity index from 1 to about 1.5. Thatcher discloses a method comprising nucleic

acid condensing peptides such as polylysine. Thatcher further discloses that polycations, such as polylysine, have a polydispersion index greater than 1.1 (i.e. column 10, lines 1-51). It would have been obvious to a person of ordinary skill in the art to modify Skjak-Braek's microcapsules by specifically utilizing a polylysine that has a polydispersity index greater than 1 because it is well known in the art that polylysine has a polydispersity index greater than 1 and thus it would desirable to utilize polylysine since it is readily available.

8. **Claim 48** is rejected under 35 U.S.C. 103(a) as being unpatentable over Skjak-Braek in view of Morrison.

The disclosure of Skjak-Braek is cited above. Skjak-Braek does not specifically disclose having a fluorescence reagent disposed in the core. Morrison discloses a microcapsule comprising an outer polymer membrane (122, fig. 1) that encloses at least two immiscible liquid phases. Morrison further discloses that one or more phases of his microcapsule comprises fluorescent molecules consisting of fluoresceins, cyanins, naturally fluorescent molecules, rhodamines, and others excited between 260 and 700 nanometers. (i.e. column 34, lines 28-41; column 23, lines 3-17). It would have been obvious to a person of ordinary skill in the art to modify Skjak-Braek's microcapsule by incorporating fluorescent molecules in the microcapsule because such molecules would provide a useful means for allowing radiological monitoring during intravascular delivery, and for enabling accurate measurements of the drug compartment volumes (i.e. Morrison, column 29, lines 31-59).

9. **Claims 1-5, 12-24, 47, and 48** are rejected under 35 U.S.C. 103(a) as being unpatentable over Zentner (US 4814183) in view of Leung et al. ("Leung," US Pub. No. 2002/0064794) and Sharma (US 5610233).

Zentner discloses a core comprising hydrogel (i.e. water insoluble, nondifussible resin entity, 2, fig. 1a); a dye disposed in the core is mobile in the core (i.e. column 5, lines 65-68); a semipermeable coating surrounding the core (i.e. cellulose acetate, column 9, line 30 to column 10, line 28); a biocompatible coating (i.e. 7, fig. 1a) surrounding the semipermeable coating; an analyte comprising glucose (i.e. column 8, lines 44-63); and the sensor is capable of detecting the analyte based on nonradiative fluorescence resonance energy transfer (i.e. column 5, lines 33-49).

Zenter does not specifically disclose having a fluorescence reagent comprising, i.e. carbocyanine dye, concanavalin A, and human serum albumin. Leung discloses in one embodiment comprising a biological polymer such as a protein that is labeled with at least a second fluorescent dye to form an energy-transfer pair (i.e. energy acceptor and an energy donor) (i.e. [0067]); carbocyanine dye having an excitation maximum at about 581 or 578 nm and an emission at about 596 or 603 nm, concanavalin A, a second carbocyanine dye having an excitation maxima at about 650 or 675 nm and an emission maxima at about 665 or 694 nm, and human serum albumin (i.e. [0004], Table 3, Example 94); and molar ratios (i.e. Table 3). It would have been obvious to a person of ordinary skill in the art to modify Zentner by incorporating a fluorescence reagent comprising an energy acceptor and an energy donor, which consists of carbocyanine dyes and albumins because it would be beneficial to have a means for monitoring the effectiveness of Zentner's invention after the consumer has digested the capsule.

Furthermore, Zentner does not specifically disclose a semipermeable coating comprising a polydisperse polymer having a weight average molecular weight from about 4 kDa to about 18 kDa and a polydispersity index greater than 1. Sharma discloses a composition comprising a

water dispersible cellulose ester having a weight average molecular weight of 10 to 60 kDa and a polydispersity index in the range of 1.05 to 2.0 (i.e. column 1, line 65 to column 2, line 9; column 3, lines 1-5). It would have been obvious to a person of ordinary skill in the art to modify Zenter's invention by utilizing Sharma's semipermeable coating because cellulose esters are known to be semipermeable and are widely used in the pharmaceutical industry.

10. **Claims 6-11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Zentner in view of Leung and Sharma ("modified Zenter"), applied to claims 1-5, 12-24, 47 above, and further in view of Tsang et al. ("Tsang," US 4663286).

The disclosure of modified Zenter is disclosed above. The modified Zenter does not specifically disclose a polydisperse polymer comprising polylysine and having a diameter from about 1 to 3 mm.

Tsang discloses a technique for encapsulating a core material within an intracapsular volume defined by a membrane. Tsang prefers encapsulating the core material with a polycationic polymer, such as polylysine, because the charge density of polycationic polymers has a material effect on porosity control of the capsules (i.e. column 2, line 65 to column 3, line 39). It would have been obvious to a person of ordinary skill in the art to modify the modified Zentner by having a semi-permeable membrane made of polylysine because it would be beneficial to have an alternate type of membrane, which is selectively permeable to solutes that are not permeable to Zentner's semipermeable membrane.

Furthermore, Tsang discloses making capsules, which preferably are between 50 microns and a few millimeters in diameter (i.e. column 5, lines 18-21). It would have been obvious to a person of ordinary skill in the art to modify the modified Zentner by making capsules which

range from 50 microns to a few millimeters in diameter because it would be easier for the consumer to ingest a relatively smaller-sized capsule.

11. **Claims 16-19 and 23-24** are rejected under 35 U.S.C. 103(a) as being unpatentable over Skjak-Braek in view of Morrison and Thatcher ("modified Skjak-Braek"), as applied to claims 1-6, 10-15, and 47 above, and further in view of Chick et al. ("Chick," US 6040194).

The modified Skjak-Braek is disclosed above. The modified Skjak-Braek does not specifically disclose a fluorescence reagent comprising albumins, and concanavalin A.

Chick discloses a fluorescent reagent comprising an energy acceptor and an energy donor (i.e. carbocyanine dyes, rhodamine dyes); and a carbocyanine dye having an excitation maximum at about 581 or 578 nm and an emission at about 596 or 603 nm, concanavalin A (i.e. glucose binding protein), a second carbocyanine dye having an excitation maxima at about 650 or 675 nm and an emission maxima at about 665 or 694 nm, and human serum albumin (i.e. glycosylated substrate). (i.e. column 2, line 30 to column 5, line 15; column 11, lines 36-47). It would have been obvious to a person of ordinary skill in the art to modify the modified Skjak-Braek, by incorporating a fluorescence reagent comprising albumin and concanavalin A because it would be beneficial to use a fluorescent reagent that is reliable, reusable, easy to use, and can be easily modified into an in vivo sensor (i.e. column 2, lines 28-30).

Response to Arguments

12. Applicant's arguments, see p. 8-11, filed 9/20/07, with respect to the rejection(s) of claim(s) 1-24 and 47-48 under the Zenter, Sharma, Wolf, Chen, Tsang, Leung, and Chick have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejections are made (see above).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lore Ramillano whose telephone number is (571) 272-7420. The examiner can normally be reached on Mon. to Fri..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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